**Example data for bootstrapping**

***Wenbo Tang***

Jadhav Lab

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This piece of data is from a project that compares hippocampal-prefrontal interactions during sleep sharp-wave ripples (SWRs) versus awake SWRs (see also Tang et al., 2017, **Fig. 3C-D**). Sharp-wave ripples are high-frequency (150-250 Hz) oscillatory events in hippocampus, lasting about 50-100 ms. SWRs occur during both waking behavior (awake SWRs) and slow-wave sleep (sleep SWRs). We asked if the neurons in the prefrontal cortex (PFC) and the hippocampus responded differently during awake vs. sleep SWRs.

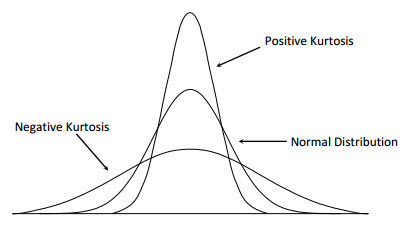
To address this question, whenever a SWR event occurred, we took the spiking activity of single prefrontal and hippocampal neurons during that event (0-500 ms after SWR onset). First, by averaging the activity across all the SWR events, we asked if their activity is strongly enhanced (i.e., excited) or suppressed (inhibited) during SWRs. We found some PFC neurons were SWR-inhibited and some were SWR-excited in both awake and sleep states, while most hippocampal neurons are SWR-excited. Further, we asked if the SWR-modulated neurons (either excited or inhibited) in these two regions responded coordinately during SWRs, which resulted in the piece of data we showed here. To do so, we took the PSTHs during SWRs of a single PFC cell and a single CA1 cell (i.e., a PFC-CA1 pair), and calculated their cross-correlation. The figure below shows the result of SWR-inhibited PFC cells paired with SWR-modulated CA1 cells during awake (*left*) and sleep SWRs (*right*):



In the figure above, each row represents the cross-correlogram of a PFC-CA1 pair. In total, we recorded 908 pairs during awake SWRs and 609 pairs during sleep SWRs. Clearly, there are more pairs show a valley time (i.e., the time lag of the valley of a cross-correlation) around 0 ms in the awake state compared to sleep, suggesting stronger synchronization between CA1 and PFC responses in the awake state. The valley times of each pairs are saved as *ValleyTime\_SWRinhpairs.mat*. In this data file, *awake* is for all pairs during awake SWRs, *sleep* is for sleep SWRs. Each value represents the valley time of a pairwise cross-correlation in *ms*. Use the sample code, *Example\_Bootstrap\_ValleyTime.m*,we can plot the distributions of valley times in both sleep and awake states:

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There are many ways to calculate if the synchronization between CA1 and PFC responses is *significantly* stronger during awake SWRs than sleep SWRs. Here, for the bootstrapping example, I would like to see if the distribution of valley times during awake SWRs (cyan bars in the figure) are *significantly* tighter around 0ms lag than that during sleep SWRs (black line in the figure). The canonical way to measure the tightness of a distribution is kurtosis (there are some caveats for the kurtosis measure, but the results are very strong here). The kurtosis is the fourth standardized moment (learn more here: <https://en.wikipedia.org/wiki/Kurtosis)>. We defined that the standard normal distribution has a kurtosis of zero. Positive kurtosis indicates a "heavy-tailed" distribution and negative kurtosis indicates a "light tailed" distribution (i.e., “tight”):



The code gives you that the kurtosis values of awake and sleep distributions are -0.28 and -1.11 respectively. Therefore, awake distribution is tighter. In fact, the result is so obvious that you can tell by eyes that awake distribution is tighter than the sleep one. However, every time when you say “A is more than B”, you need to attach a p-value. Therefore, how to get a p-value for this comparison, because you can only get one kurtosis for one distribution, and there is no well-established statistic method to test two kurtosis values (as far as I know). So, we turn to bootstrap. Also, to overcome the unequal sampling (the awake case has more pairs), we can resample the awake data with the same number of pairs as in sleep data.

To do bootstrap, I randomly took 609 pairs from awake and sleep data respectively with replacement, calculated a kurtosis for each of the resampled data, and compared which one is larger. I repeated these steps 1000 times, so I have 1000 kurtosis values for each case, and did 1000 comparisons. The distributions of these kurtosis values are shown below (your distributions may look slightly different because of the random sampling procedure):



The blue line is the kurtosis of the original sleep distribution (i.e., -1.1), the black line is the kurtosis of the original awake distribution (i.e., -0.28). You can see that these two distributions are not overlapped with each other at all, that is the awake kurtosis is always larger than the sleep one. Therefore, the p-value for this statistic is 0.